**IN THE SPECIFICATION:**

Please amend the specification as shown:

**Page 6, line 29 through Page 7, line 20**: Please replace the paragraph with the following amended paragraph:

Non-metabolic actions of amylin include vasodilator effects which may be mediated by interaction with CGRP vascular receptors. Reported [[in vivo]] *in vivo* tests suggest that amylin is at least about 100 to 1000 times less potent than CGRP as a vasodilator (Brain [[et al.]] *et al.*, *Eur. J. Pharmacol.*, 183:2221 (1990); Wang [[et al.]] *et al.*, *FEBS Letts.*, 291:195-198 (1991)). The effect of amylin on regional hemodynamic actions, including renal blood flow, in conscious rats has been reported (Gardiner [[et al.]] *et al.*, *Diabetes*, 40:948-951 (1991)). The authors noted that infusion of rat amylin was associated with greater renal vasodilation and less mesenteric vasoconstriction than is seen with infusion of human α-CGRP. They concluded that, by promoting renal hyperemia to a greater extent than did α-CGRP, rat amylin could cause less marked stimulation of the renin-angiotensin system, and thus, less secondary angiotensin II-mediated vasoconstriction. It was also noted, however, that during [[coninfusion]] coinfusion of human α-$^{8-37}$CGRP (SEQ ID NO: 18) and rat amylin, renal and mesenteric vasoconstrictions were unmasked, presumably due to unopposed vasoconstrictor effects of angiotensin II, and that this finding is similar to that seen during coinfusion of human A-CGRP and human α-$^{8-37}$CGRP ([[id.]] *id.* at 951).

**Page 12, lines 5-9:** Please replace the paragraph with the following amended paragraph:

We have now discovered, surprisingly, that amylin and amylin agonists, for example, the amylin agonist analogue $^{25,28,29}$Pro-h-amylin (also referred to as "pramlintide" and previously referred to as "AC-0137") (SEQ ID NO: 12), can be used for treatment of obesity in humans.

**Page 12, lines 10-29:** Please replace the paragraph with the following amended paragraph:

The present invention is directed to novel methods for treating or preventing obesity in humans comprising the administration of an amylin or an amylin agonist, for example, the amylin agonist analogue $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12). The amylin or amylin agonist may be administered alone or in conjunction with another obesity relief agent. In one aspect, the invention is directed to a method of treating obesity in a human subject comprising administering to said subject an effective amount of an amylin or such an amylin agonist. By "treating" is meant the management and care of a patient for the purpose of combating the disease, condition or disorder, and includes the administration of an amylin or an amylin agonist to prevent the onset of symptoms or complications, alleviating the symptoms or complications, or eliminating the disease condition or disorder. Treating obesity [[therefor]] therefore includes the inhibition of weight gain and inducing weight loss in patients in need thereof. Additionally, treating obesity is meant to include controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance.

**Page 13, lines 23-28:** Please replace the paragraph with the following amended paragraph:

In a preferred embodiment, the amylin agonist is an amylin agonist analogue, preferably, $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12). $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12) and other amylin agonist analogues are described and claimed in U.S. Patent No. 5,686,411, issued November 11, 1997, the contents of which are also hereby incorporated by reference.

**Page 13, line 29 through Page 14, line 6:** Please replace the paragraph with the following amended paragraph:

In another aspect, the present invention is directed to novel methods of reducing insulin-induced weight gain in human subjects who are taking insulin by administering a therapeutically effective amount of an amylin or an amylin agonist. In one embodiment, the subject has diabetes mellitus, for example, type 1 or type 2 diabetes mellitus. In a preferred embodiment, the amylin agonist is $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12).

**Page 14, lines 10-25**: Please replace the paragraph with the following amended paragraph:

The study described in Example 1 showed that administration of the amylin agonist $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12) (pramlintide) to insulin-using diabetics (type 2) resulted in a decrease in body weight after 4 weeks which achieved statistical significance within two dosage groups, 60 μg TID and 60 μg QID. The study described in Example 2 showed that administration of pramlintide (30 μg or 60 μg QID) to type 1 diabetes resulted in a statistically significant decrease in body weight, compared to placebo, at 13, 26 and 52 weeks. The study described in Example 3 showed that administration of pramlintide (30, 75 or 150 μg TID) to patients with type 2 diabetes who require insulin resulted in a [[statisticaly]] statistically significant decrease in body weight, compared to placebo, at 13, 26 and 52 weeks. These results are in sharp contrast to treatment with insulin alone in patients with type 1 or type 2 diabetes, which is usually associated with weight gain.

**Page 15, lines 1-2:** Please replace the paragraph with the following amended paragraph:

1. An agonist analogue of amylin having the amino acid sequence (SEQ ID NO: 14):

**Page 16, lines 1-2:** Please replace the paragraph with the following amended paragraph:

2. An agonist analogue of amylin having the amino acid sequence (SEQ ID NO: 15):

**Page 17, lines 5-6:** Please replace the paragraph with the following amended paragraph:

3. An agonist analogue of amylin having the amino acid sequence (SEQ ID NO: 16):

**Page 18, lines 4-5:** Please replace the paragraph with the following amended paragraph:

4. An agonist analogue of amylin having the amino acid sequence (SEQ ID NO: 17):

**Page 19, lines 3-5:** Please replace the paragraph with the following amended paragraph:

Preferred amylin agonist analogues include $^{25,28.29}$Pro-h-amylin (SEQ ID NO: 12), $^{18}$Arg$^{25,28,29}$Pro-h-amylin (SEQ ID NO: 10) and $^{18}$Arg$^{25,28}$Pro-h-amylin (SEQ ID NO: 8).

**Page 27, lines 17-30**: Please replace the paragraph with the following amended paragraph:

The effective single, divided or continuous analgesic doses of the compounds, for example, including $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12), $^{18}$Arg$^{25,28,29}$Pro-h-amylin (SEQ ID NO: 10) and $^{18}$Arg$^{25,28}$Pro-h-amylin (SEQ ID NO: 8) will typically be in the range of about 0.01 to about 5 mg/day, preferably about 0.05 to about 2 mg/day and more preferably about 0.1 to 1 mg/day, for a 70 kg patient, administered in a single, divided or continuous doses. The exact

dose to be administered is determined by the attending clinician and is dependent upon a number of factors, including, these noted above. Administration should begin at the first sign of obesity. Administration may be by injection or infusion, preferably intravenous, subcutaneous or intramuscular. Orally active compounds may be taken orally, however, dosages should be increased 5-10 fold.

**Page 28, line 26 through page 29, line 20:** Please replace the paragraph with the following amended paragraph:

Study participants were males and females 25 to 78 years of age with a history of Type II diabetes mellitus requiring treatment with insulin for at least 6 months prior to the pre-screening visit. Patients had a body weight not varying more than 45% from the desirable weight before admission into the study (based upon Metropolitan Life Tables). The study employed methods described in Thompson [[et al., Diabetes]] *et al., Diabetes*, 46:632-636 (1997). Following a placebo lead-in period, patients were randomized to receive placebo or one of three dose regimens of $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12) (pramlintide) for 4 weeks: 30 μg QID (before breakfast, lunch, dinner and evening snack), 60 μg TID (before breakfast, lunch and dinner) or 60 μg QID (before breakfast, lunch, dinner and evening snack). Throughout the study drug period, patients self-administered four injections of study drug daily, within 15 minutes of each meal and the evening snack. During the double-blind period, patients randomized to pramlintide 60 μg TID administered placebo before the evening snack. Both pramlintide and placebo were administered as separate injections into the subcutaneous tissue of the anterior abdominal wall; the specific site was alternated after each injection. Patients were instructed to remain on their usual diet, insulin and exercise regimens throughout the study, unless otherwise instructed by the investigator, and to abstain from alcoholic beverages prior to all clinic visits.

**Page 40, lines 3-18:** Please replace the paragraph with the following amended paragraph:

[[**Preparation of $^{25,28,29}$Pro-h-Amylin**]] Preparation of $^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 12)

Solid phase synthesis of $^{25,28,29}$Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and $N^{a}$-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The $^{2,7}$-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{25,28,29}$Pro-h-amylin (SEQ ID NO: 12) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,949.

**Page 40, line 21 through Page 41, line 6:** Please replace the paragraph with the following amended paragraph:

[[**Preparation of $^{18}$Arg$^{25,28,29}$Pro-h-Amylin**]] Preparation of $^{18}$Arg$^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 10)

Solid phase synthesis of $^{18}$Arg$^{25,28,29}$Pro-h-amylin (SEQ ID NO: 10) using methylbenzhydrylamine anchor-bond resin and $N^{a}$-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The $^{2,7}$-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{18}$Arg$^{25,28,29}$Pro-h-amylin (SEQ ID NO: 10) was purified by preparative reversed-phase HPLC. The peptide was found to

be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3,971.

**Page 41, lines 9-24:** Please replace the paragraph with the following amended paragraph:

[[**Preparation of $^{18}Arg^{25,28}Pro$-h-Amylin**]] Preparation of $^{18}Arg^{25,28}Pro$-h-Amylin (SEQ ID NO: 8)

Solid phase synthesis of $^{18}Arg^{25,28}Pro$-h-amylin (SEQ ID NO: 8) using methylbenzhydrylamine anchor-bond resin and $N^a$-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The $^{2,7}$-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{18}Arg^{25,28}Pro$-h-amylin (SEQ ID NO: 8) was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3,959.

**Page 42, lines 4-10**: Please replace the paragraph with the following amended paragraph:

Evaluation of the binding of compounds to amylin receptors was carried out as follows. $^{125}$I-rat amylin (SEQ ID NO: 19) (Bolton-Hunter labeled at the N-terminal lysine) was purchased from Amersham Corporation (Arlington Heights, IL). Specific activities at time of use ranged

from 1950 to 2000 Ci/mmol. Unlabeled peptides were obtained from BACHEM Inc. (Torrance, CA) and Peninsula Laboratories (Belmont, CA).

**Page 42, line 24 through Page 43, line 10:** Please replace the paragraph with the following amended paragraph:

To measure $^{125}$I-amylin (SEQ ID NO: 20) binding, membranes from 4 mg original wet weight of tissue were incubated with $^{125}$I-amylin (SEQ ID NO: 20) at 12-16 pM in 20 mM HEPES buffer containing 0.5 mg/ml bacitracin, 0.5 mg/ml bovine serum albumin, and 0.2 mM PMSF. Solutions were incubated for 60 minutes at 23°C. Incubations were terminated by filtration through GF/B glass fiber filters (Whatman Inc., Clifton, NJ) which had been presoaked for 4 hours in 0.3% polyethyleneimine in order to reduce nonspecific binding of radiolabeled peptides. Filters were washed immediately before filtration with 5 ml cold PBS, and immediately after filtration with 15 ml cold PBS. Filters were removed and radioactivity assessed in a gamma-counter at a counting efficiency of 77%. Competition curves were generated by measuring binding in the presence of $10^{-12}$ to $10^{-6}$ M unlabeled test compound and were analyzed by nonlinear regression using a 4-parameter logistic equation (Inplot program; GraphPAD Software, San Diego).

**Page 46, lines 6-25:** Please replace Table VIII with the following amended Table VIII:

TABLE VIII

| Muscle $EC_{50}$ (nM) | | Receptor Binding Assay $IC_{50}$ (pM) | Soleus Assay |
|---|---|---|---|
| 1) | $^{25}Pro^{26}Val^{28,29}Pro$-h-Amylin (SEQ ID NO: 1) | 18.0 | 4.68 |
| 2) | $^{2,7}$Cyclo-[$^{2}$Asp,$^{7}$Lys]-h-Amylin (SEQ ID NO: 2) | 310.0 | 6.62 |
| 3) | $^{2-37}$h-Amylin (SEQ ID NO: 3) | 236.0 | 1.63 |
| 4) | $^{1}$Ala-h-Amylin (SEQ ID NO: 4) | 148.0 | 12.78 |
| 5) | $^{1}$Ser-h-Amylin (SEQ ID NO: 5) | 33.0 | 8.70 |
| 6) | $^{25,28}$Pro-h-Amylin (SEQ ID NO: 6) | 26.0 | 13.20 |
| 7) | des-$^{1}$Lys$^{25,28}$Pro-h-Amylin (SEQ ID NO: 7) | 85.0 | 7.70 |
| 8) | $^{18}Arg^{25,28}$Pro-h-Amylin (SEQ ID NO: 8) | 32.0 | 2.83 |
| 9) | des-$^{1}$Lys$^{18}Arg^{25,28}$Pro-h-Amylin (SEQ ID NO: 9) | 82.0 | 3.77 |
| 10) | $^{18}Arg^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 10) | 21.0 | 1.25 |
| 11) | des-$^{1}$Lys$^{18}Arg^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 11) | 21.0 | 1.86 |
| 12) | $^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 12) | 10.0 | 3.71 |
| 13) | des-$^{1}$Lys$^{25,28,29}$Pro-h-Amylin (SEQ ID NO: 13) | 14.0 | 4.15 |